

Amendment A
Inventor: Neil A. Winegarden
Attorney Docket No.: 718188.1

REMARKS

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE".

The specification has been amended to correct clerical errors, no new matter has been introduced.

The elected pending claims 1 - 17 have been deleted and replaced with new claims 44 - 89.

Support for the new claims is found in the originally filed claims and application.

The Drawings

The Examiner has object to the drawings as being informal. Formal drawings will be provided upon receipt of an indication of allowable subject matter.

Specification

The Examiner objected that the specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Revised paragraphs with corrected errors are included in this response.

The Examiner also objected that the use of the trademark TeleChem Chipmaker 2 and TeleChem Chipmaker 3 should be capitalized wherever it appears and be accompanied by the generic terminology. The trademark is capitalized and accompanied by the generic terminology "pins" in the application on pages 2 and 9. The trademark has been deleted from the claims.

Claim Objections

Claims 5-7, 12-14 and 17 were objected to under 37 CFR 1.75(c) as being improper form because a multiple dependent claim cannot depend from any other multiple dependent claim.

The multiple dependency has been removed by deletion of the aforementioned claims and all the claims may be further treated on the merits.

Claim Rejections – 35 USC 112

Claims 1-4, 8-11, 15 and 16 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Examiner alleged a lack of positive recitement and antecedent basis for “the spotting members.” The new claims avert this objection by either reciting spotting members as a positive element or by providing an antecedent basis.

Claim 1 was rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. The alleged omitted structural cooperative relationships are: microarray spotting members, plate, structure for coupling, and vacuum manifold. The new claims overcome this objection. For example, claim 44 recites a plate defining a plurality of fluid flow apertures and turbulence means for creating turbulence between the spotting members and the apertures for removing liquid from the first open end portions of the spotting members through the apertures. For other claims, such as claim 75, which include wording similar to the allegedly objectionable wording, it is submitted that the relationships are

Amendment A
Inventor: Neil A. Winegarden
Attorney Docket No.: 718188.1

properly defined, for example, by reference to structure for coupling the plate to communicate with a source of vacuum to draw fluid from the microarray spotting members through the fluid flow channel members. The structure for coupling permits the vacuum to draw fluid from the spotting members into the channel members. If the Examiner continues to find the wording objectionable, Applicants request that the objection in the last line of paragraph 10 of the Office Action be restated because there appears to be a grammatical misstatement that makes the sentence difficult to understand.

The Examiner objected to claim 2 on the basis that it was unclear whether the apertures are arranged in parallel rows from the perspective of a cross section or a top view. Claim 47, which refers to parallel rows, depends from claim 47 to better define the parallel rows. For other claims, Applicants submit that it is clear to a person reading the claims in light of the specification that the apertures are parallel from the perspective of a top view.

The Examiner also stated that for claim 3, the specification has not sufficiently defined pins. Claim 3 has been deleted, but other claims refer to pins. The Applicants submit that this term is sufficiently defined in the context of the specification which includes particular examples of pins, such as the TeleChem Chipmaker 2 and TeleChem Chipmaker 3.

References to the TeleChem Chipmaker 2 and TeleChem Chipmaker 3 in claims have been deleted.

The Examiner objected to claim 8, on the basis that the claim is incomplete and contains a gap between the steps under 35 USC 112 because it is not stated exactly how liquid is removed

Amendment A
Inventor: Neil A. Winegarden
Attorney Docket No.: 718188.1

by a vacuum and moving the spotting members up and down. New claims 45, 56, 61-69 and 83-88 refer to reciprocation. Claim 44 describes a turbulence means, which in claim 45 is defined as including an aligning means and a reciprocating means. It is submitted that the nature of the way that a vacuum and moving the members up and down removes liquid is clear from the claim wording in view of the specification. Preferably, a vacuum source creates a downward flow of air to be drawn into the manifold. This rapid flow of air streams over the pins and through the slit in the spotting members. As the air flows, any liquid contained in the slit of the spotting members is drawn out and into the manifold and vacuum chamber. By reciprocating the spotting members up and down from the manifold, a higher degree of air turbulence is created to ensure that more air flows through the slit of the spotting member and not just simply flowing past the pin. This reciprocating motion aids in drying and cleaning of the spotting members and improves its function. The small size of the holes ensures a high degree of airflow and also that the airflow is concentrated at the tip of the spotting member, where the liquid is present. The Examiner objected to claims 9-11 on the basis that the term "reciprocation" should be further defined with specific upward or downward movement. The Applicants submit that the amount of upward or downward movement is defined by the claims in view of the specification (e.g. page 9) and would be clearly understood by a skilled person based on the wording in the new claims.

The Examiner objected to claims 15 and 16 on the basis that they depend from claim 1 which is not a method claim. Claims 15 and 16 have been deleted and the noted dependency

does not occur in the new claims.

Claim Rejections - 35 USC 102

Claims 1-3 were rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/40383 by Gavin et al. The Examiner stated that Gavin et al. disclose a vacuum manifold (160) for use in removing liquid from microarray spotting members or pins (162)(see FIGS. 1-4, 15 and 16; PAGE 11, lines 25-30; PAGE 19, lines 16-26; PAGE 20, lines 23-25). A plate (174) defining a plurality of fluid flow channel members (176) formed through the plate (174)(see FIG. 16; PAGE 20, lines 19-21). Each channel member has an inlet and outlet in fluid communication (see FIG. 16). The channel members (176) are arranged in parallel rows (see FIGS. 5, 5A, 10, 15, and 16). A structure couples the plate to communicate with a source of vacuum to draw fluid from the microarray spotting members or pins (162) through the fluid flow channel members (see FIGS. 5A, 7-9, 11, 11A, 11B, 12, 12A, 12B, 15, 16; PAGE 19, 20-26). The Examiner concludes that Gavin et al. includes all the limitations in claims 1-3.

The deletion of claim 1 and insertion of new claims render the rejection moot. The devices described in Gavin et al. are not used for manufacture of microarrays. The Examiner will see that the arrangement of the Gavin et al. device and the way in which it operates are completely different from the Applicants' device. Gavin et al. does not disclose a manifold including a plate, the plate defining a plurality of fluid flow apertures extending through the plate, the apertures having an axis and a first diameter, the spotting member bodies having a second diameter wherein the second diameter is greater than the first diameter, and wherein the

first open end portion of the spotting member is adapted to extend into the aperture; and turbulence means for creating turbulence between the spotting members and the apertures for removing liquid from the first open end portions of the spotting members through the apertures. The limitation of the other new claims are also not taught by Gavin et al.

The system in Gavin et al. is devised to handle solid supports (beads) which are coupled to chemicals of interest. It presents a method for processing a plurality of these supports. The beads are “arrayed” into microwell plates, not onto a microarray slide. A microarray slide is typically a solid planar substrate such as a microscope slide. Brief comments on Gavin et al. follow.

- 1) The Gavin et al. system uses a set of lumens (preferably needles) which are hooked up to a vacuum system to attract the beads to the lumens. The vacuum is created within or applied to the lumen to draw gas through the lumen and draw a solid support 24 onto an end of the lumen (p.10, l. 25-29) which is used to load the lumens, not clean them. Gavin et al. does not teach a device that removes liquid from the first open end portion of a spotting member through apertures in a plate.
- 2) Pressure is then applied by the Gavin et al. device to the lumens to cause them to eject both the solid support (bead) and any excess liquid that may have been taken up as well. Thus the lumen has both a proximal and distal opening allowing fluid communication. The spotting members used in the invention and taught in the application are not such devices. The invention uses solid pins with a microslit in the tapered end, such as the

Telechem Chipmaker 2 pins or Telechem Chipmaker 3 pins.

- 3) After ejecting the bead and the liquid, the lumens are still not clean, and are cleaned with methanol. Thus a turbulence means or vacuum is not being used to clean the lumens.
- 4) No mention is made of any of: a manifold assembly to remove liquid from microarray spotting members (e.g. pins); the spotting members themselves, or the relative size of apertures.

The Examiner referenced a number of figures and passages of Gavin, et al. which are not relevant to the new claims. These portions of Gavin et al. are discussed below.

- a. Figures 1-4 (and page 11, lines 25-30) show how the lumen is lowered into the well of a microwell plate containing beads. Presumably a vacuum is applied to the distal end of the lumen to attract a bead to the lumen. The hole in the lumen is smaller than the size of the bead thus when the bead is attracted to the lumen, it closes off the aperture. A pressure differential keeps the bead attracted onto the lumen. The lumen is then removed from the microwell with bead attached. The lumen is then maneuvered to a second microwell plate where pressure is applied to the distal end of the lumen to cause the bead to be ejected.
- b. Figure 15 (and page 19, lines 19-26) describes a disposable plate of lumens. This plate essentially replaces the pins and needles described earlier in this patent application. The plate is disposable and thus does not need to be cleaned. It is meant to pick up a plurality of solid supports and transfer them to a solid reactive

surface (such as a plate of bacteria) to monitor the effect of the chemicals attached to the beads. The plate is very different than the manifold assembly and other claimed aspects of the invention.

- c. Figure 16 (and page 20 lines 23-25) shows how the plate described in Figure 15 can then be introduced (coupled) to a microwell plate such that each of the reactions is keep separate from one another. Again, the plate comprising the lumens is a transfer apparatus, not a mircoarray spotting member.
- d. Figures 5 and 5A show how the lumens would be arranged in a parallel row. Again, these lumens are hollow and they themselves are a transfer apparatus in communication with the vacuum source to allow suction through the channels.
- e. Figure 10 shows the arrangement of bead source and target plates. It is a platform with several well plates on it.
- f. Figures 7-9 show how the lumens are designed and coupled to a vacuum source.
- g. Figures 11-12 show an alternative configuration of the capillary array (not just a single parallel line of capillaries).

Thus, Gavin et al clearly does not disclose the claimed invention. As noted above, Gavin does not disclose a manifold assembly or any of the other claimed devices or methods. It also does not disclose use of microarray spotting members. It also does not disclose apertures having a 1st diameter and spotting members having a 2nd diameter greater than the 1st diameter. It also does not create turbulence between the spotting members and the apertures to remove liquid

Amendment A
Inventor: Neil A. Winegarden
Attorney Docket No.: 718188.1

from the spotting members.

Claim Rejections - 35 USC 103

Claim 4 was rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/40383 to Gavin et al. The Examiner stated, referring to claim 4, that Gavin et al. do not explicitly disclose the use of TeleChem Chipmaker 2 pins, TeleChem Chipmaker 3 pins, or a combination thereof. It was further stated that, it would have been obvious to one having ordinary skill in the art to modify the device of Gavin et al. to use a specific brand of pins by TeleChem as they are disclosed by the Applicant as commercially available.

For similar reasons as those stated with respect to the objection under 35 USC 102, the invention is also not obvious in view of Gavin et al. The Applicants also submit that the TeleChem pins are not able to perform the function described in the Gavin et al. patent. Gavin et al. discloses a device that requires hollow lumens to function. The TeleChem pins are not hollow through their entire length. A primary difference is the mode of action of the spotting members of the invention compared to Gavin et al.'s "transfer members". In Gavin et al., beads are being sucked onto the aperture of the lumen by means of vacuum. In Applicants' invention, capillary action draws liquid into the slit of a spotting member (e.g. a tapered pin), and then the pins function similar to an ink stamp when spotting. Because the Applicants' spotting members are not hollow through their entire length, Applicants invented a highly effective method of cleaning the pins.

To establish obviousness, the Examiner must make out a *prima facie* case that satisfies

Amendment A
Inventor: Neil A. Winegarden
Attorney Docket No.: 718188.1

three requirements: 1) the references must teach or suggest all the claim limitations; 2) the prior art combined with general knowledge must include a suggestion or incentive to modify or combine the references and 3) the modification or combination must have a reasonable chance of success. The cited references do not teach or suggest all of the claim limitations. For example, Gavin, et al. do not disclose a manifold assembly for removing liquid from microarray spotting members. It also does not disclose the 1st and 2nd diameters and the turbulence means. In paragraph 24 of the Office Action, claims 8 and 9 were rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/40383 to Gavin et al. in view of U.S. Patent No. 5,935,895 to Elliot et al. Thus, Gavin, et al. cannot support an obviousness rejection.

The Examiner stated, referring to claim 8, that Gavin et al. disclose applying a source of vacuum to the manifold to remove liquid from microarray spotting members (see page 19, lines 20-26). The Examiner stated that Gavin et al. do not disclose reciprocating the spotting members to create air turbulence between the spotting members and the inlets. The Examiner also alleged that Elliott et al. disclose a robot arm assembly (12) to move the microarray spotting members proximate to the inlets (26, 28, 30, 32) such that the members are concentric with the inlet during reciprocation (see ABSTRACT, FIGS. 1 and 4; COL. 3, lines 28-24 and 57-61. The Examiner suggests that moving the spotting members would provide more control over the alignment of the members with the inlets and that the vertical movement of the spotting members toward the inlets would create air turbulence between the spotting members and inlets. The Examiner then concludes that it would have been obvious to one having ordinary skill in the art at the time the

invention was made to modify the device of Gavin et al. to reciprocate the spotting members as in Elliott et al. to provide more control over the alignment with the inlets.

The failure of Gavin, et al. to disclose or suggest the elements of the new claims is described above. Elliot, et al. also do not disclose or suggest these elements. Further, the combination of these two references does not disclose or suggest the new claim limitations. Gavin et al. do not disclose a turbulence means or use of a source of vacuum on the manifold to remove liquid from the spotting members. In Gavin et al., the vacuum is intended to add liquid to the members, and pressure is used to remove it. Secondly the system must be a closed system, thus the members and manifold cannot be decoupled. If they were reciprocated away from one another, the device of Gavin et al. would cease to function because it would lose the vacuum/pressure in the lumens.

Elliott et al. refer to a robotic arm. Again, this system is for a microwell plates of beads, one bead per well. This is a standard liquid handler adapted to hold needles much as described in Gavin et al. These needles function the same as those described in Gavin et al. Several passages of Elliott, et al. were identified by the Examiner and these passages are discussed below.

- 1) The Examiner cites the ABSTRACT. The ABSTRACT makes no mention of turbulence means, a vacuum manifold, or reciprocation. Also it does not refer to inlets.
- 2) Figure 1 is a picture of the liquid handling robot. There is no turbulence means or vacuum.

- 3) Figure 4 shows how a syringe pump on an actuator is used to draw liquid into the hollow lumen of the needle thus attracting a bead to the aperture. Also on a Y-connector there is an air supply which is required to force the liquid out of the needle and eject the bead.
- 4) Items 26, 28, 30, and 32 are wells of a microwell plate, not inlets of a vacuum manifold. Thus, the needles are being moved such that they are concentric with the wells of a microwell plate, not a manifold.
- 5) There is no mention of reciprocation. A separate tube entering the well provides a stream of air that causes bubbles which keep the beads suspended in solution and this is not a turbulence means for removing liquid from the first open end portions of the spotting members. The spotting members or needles are not reciprocated in the well.

The Examiner refers to reciprocation to align members with inlets. In the Applicants' invention, reciprocation is to remove liquid from the spotting members rather than to align members with inlets. The high precision of the robot allows the Applicants to address a particular location. The robot is instructed to move to a specific set of X, Y and Z coordinates which causes the tips of the "spotting members" to be concentric with the apertures of the vacuum manifold. Z-axis reciprocation is then used to increase air turbulence causing more effective withdrawal of solution from the spotting members.

Claim 10 was rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/40383 to Gavin et al. in view of U.S. Patent No. 5,935,859 to Elliott et al. and U.S. Patent No. 4,439,526 to Columbus et al. The Examiner stated, referring to claim 10, that Gavin et al. in

view of Elliott et al. do not explicitly disclose that the spotting members are about 100 micrometers from the inlet prior to reciprocation. It was further stated that Columbus discloses that useful spacing distance is between 50-600 microns between the members (16) and (18) to form a capillary transport passage (20) between opposing surfaces (24) and (26)(COL. 3, lines 37-51). It was alleged that discovering the optimum value of a result effective variable, such as the distance between the members and inlet for a certain drop size, requires only routine skill in the art (*In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980)). The Examiner concluded that it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Gavin et al. in view of Elliott et al. to select an optimum spacing distance of 100 microns for the desired drop size within the range of 50-600 microns of Columbus.

The applicants have noted above the many differences between the invention in the new claims and Gavin et al. and Elliott et al.

The Applicants are not claiming in relation to drop size. As well, Columbus et al. use a very different technology involving a device for capillary transport of liquid along a passage. It is used for loading diagnostic equipment. The device is loaded by placing a drop of fluid on an inlet port. That liquid is drawn into the inlet port by capillary action into the channel of the device (made by two opposing surfaces at a particular spacing in the range of 50 to 600 micrometers). This is not related to bringing the spotting member (preferably a pin) in proximity to the inlet port of a vacuum manifold. It is unrelated to microarrays and spotting. Columbus et

Amendment A
Inventor: Neil A. Winegarden
Attorney Docket No.: 718188.1

al. relates to loading a liquid sample into a capillary device. There is no motivation or suggestion to combine Columbus et al with the other references. The Applicants further submit that these references do not disclose or suggest all the claim limitations.

Claim 11 was rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/40383 to Gavin et al. in view of U.S. Patent No. 5,935,859 to Elliott et al. and U.S. Patent No. 6,245,297 to Kowallis.

The Examiner stated that Gavin et al. in view of Elliott et al. do not explicitly disclose that the spotting members are reciprocated about a distance of 1 mm. The Examiner states that Kowallis discloses that the spacing distance between the members and the substrate is less than about 2 mm, which encompasses the sum of the reciprocation distance of 1 mm from the original distance of 100 microns (see COL 13, lines 59-63). It was further stated that discovering the optimum value of a result effective variable, such as the reciprocation distance between the members and inlet for a certain drop size, requires only routine skill in the art (*In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980)). The Examiner concluded that it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Gavin et al. in view of Elliott et al. to select an optimum reciprocation distance of 1 mm for the desired drop size that is less than 2mm as taught by Columbus, et al.

The differences between Gavin et al., Elliott et al and the present invention were described in detail above. The devices described in Gavin et al and Elliott et al. are not for manufacture of microarrays. The Kowallis application refers to the manufacture of microarrays.

The Kowallis invention relates to a conveyor belt system for manoeuvring plates back and forth on the robotic system. Kowallis is discussed in more detail below.

- 1) Kowallis mentions the importance of cleaning the tips and drying. Kowallis also mention that the tips enter at least partially into an aperture and that water flows over the tips.

Then a dry warm gas is passed over the tips to dry them. Kowallis is not using a vacuum to dry the tips, but rather a gas under pressure. Kowallis makes no mention of the design of a manifold and there appears to be no vacuum manifold on this system. There appears to be no mention of a plurality of spotting members in Kowallis.

- 2) The holes that are used to wash and dry the tips are empty holes where microtubes could be placed. As a result the aperture must be much larger than the spotting members (see e.g. figs. 4 and 5).

- 3) The 2mm limitation on distance is specifically during the action of spotting, not cleaning. It mentions that the stroke should be less than 2 mm and thus the tips are 2 mm from the substrate (i.e. glass slide). This has nothing to do with a manifold for cleaning spotting members.

- 4) In addition, Applicants' emphasize that they are not claiming drop sizes. The claims are directed toward removing the excess, remaining liquid (solution or wash solution) from the spotting members.

Claims 15 and 16 were rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/40383 to Gavin et al. in view of U.S. Patent No. 6,416,713 to Ford et al.

Amendment A
Inventor: Neil A. Winegarden
Attorney Docket No.: 718188.1

Referring to claim 15, the Examiner states that Gavin et al. do not explicitly disclose that the vacuum is created by a compressed air system providing a pressure between 50 and 90 psi. Ford et al. disclose that a vacuum can be created by a compressed air system of up to 90 psi (see col 14, lines 65 and 66). The Examiner also states that discovering the optimum range or workable range, such as the pressure provided by a compressed air system for a certain flow rate, requires only routine skill in the art (In re Aller, 105 USPQ 233). The Examiner concluded that it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Gavin et al. to determine an optimum range of pressure provided by the compressed air system for the desired flow rate of liquid that is less than 90 psi as taught by Ford et al.

The difference between Gavin et al. and the claimed invention are described above.

Ford et al. do not disclose that compressed air can cause a vacuum or turbulence. In fact the pressure is used to pressurize reagent bottles. Those bottles once under pressure (not vacuum) will then allow the free flow of liquid out of the dispenser cap. Ford et al are not using a turbulence means or vacuum. This system is an automated biological reaction system (for immunostaining). It is a means of dispensing liquids onto slides in bulk. It does not involve microarrays, spotting members or vacuum manifolds.

The Examiner also provided art made of record and not relied upon on the basis that the art was considered pertinent to Applicants' disclosure and includes one or more limitations in the claims. Applicants respectfully disagree that the art is pertinent and further state that the art does

Amendment A
Inventor: Neil A. Winegarden
Attorney Docket No.: 718188.1

not disclose limitations in the new claims.

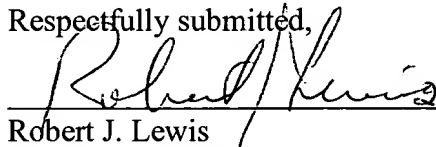
Based on the foregoing remarks, the Applicants respectfully request withdrawal of the Examiner's rejections and objections.

It is now believed that all of the pending claims in the present application, namely, claims _____ contain limitations and restrictions which patentably distinguish them over the cited prior art. None of the cited references, either alone or in any combination thereof disclose or suggest all of the novel features associated with the present _____ as explained above, nor do the referenced constructions provide the specific advantages and objectives obtained by the present device. Favorable action and allowance of the claims is therefore respectfully requested.

If any issue regarding the allowability of any of the pending claims in the present application could be readily resolved, or if other action could be taken to further advance this application such as an Examiner's amendment, or if the Examiner should have any questions regarding this amendment, it is respectfully requested that Examiner please telephone Applicants' undersigned attorney in this regard.

Date: 4/03/03

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE
MARKED-UP DRAFT OF AMENDMENT

Please replace the paragraph on page 7, lines 23-27 with the following

Figure 5: Side view of a manifold with micro apertures. One preferably sets the robot up such that the pin tip just passes the opening of the hole at the down position (A), and is reciprocated up to a position a few hundred microns above the opening (B). Reciprocation [An reciprocation] up and down is used to increase air turbulence, increasing the cleaning efficiency.

Please replace the paragraph on page 9, lines 5-15 with the following:

Significantly improved cleaning is achieved by using this vacuum manifold 4. First, the inlets (holes/apertures) of the vacuum manifold are reduced in cross-sectional area. Alternatively, the inlets may be effectively reduced by placing a piece of sticky aluminum foil over the manifold and making new holes with a 28 gauge needle, or with an off-spec spotting pin (Figure 2) [(Figures 2)]. Alternatively, the manifold could be constructed with smaller apertures 3 (Figure 2) [(Figures 2)]. The magnitude of reduction of the cross-sectional area is preferably such that only a portion (for example, approximately half) of the pin tip 1 could fit through the aperture 3 and the pin body 2 cannot enter the aperture. Secondly, the pins 2 are preferably set to be about 100 micrometers above the manifold. From this point the pins 2 are reciprocated up and down to create further air turbulence, which result in excellent cleaning (3 to 5 percent carryover at maximum).

Please replace the paragraph on page 12, lines 10-15 with the following:

During printing onto the slides 9 it is necessary to both approach and depart from the slides 9 at a relatively slow speed in order to promote [order promote] optimal spot quality. If the pins 2 approach the slide 9 too quickly they will create “micro splashes” which will disrupt

spot morphology. Similarly, if the pins 2 are pulled away from the slide 9 too quickly, then the spots can be pulled in such a way [such away] that morphology is disrupted. The following exemplary aspects were determined:--

Please replace the paragraph on page 13, line 31 to age 40, line 10 with the following:

This procedure leads [This procedure lead] to ideal spot morphology with one particular set up (3X SSC spotting solution, DNA concentration of 0.1 to 0.2 micrograms/microlitre), however differing spotting solutions and DNA concentrations require different timings due to changes in viscosity. To a person in the art, it is clear that variations to the mentioned parameters may also be used for proper performance, for example the extent that the pins are allowed to drop past touching the slide (approximately 200 micrometers in this case), the height of the pins in the “up position” (about 2 mm above the “down position”), and the duration the pin rests on the slide. These numbers are offered as examples. Lower viscosity solutions are likely to splash more easily but will make larger spots. As a result it is generally preferred that (1) the approach speed be reduced; (2) the distance past touching be reduced; and (3) the departure speed be reduced. Typically higher viscosity solutions will have (1) the distance past touching increased to increase dwell time; or (2) an additional step to provide a dwell time of defined duration after touching. With higher viscosity solutions approach and departure speeds can be increased which will compensate for the required dwell time.

Please replace the paragraph on page 14, lines 14-24 with the following:

It is important that deposition of probe DNA yield regularly spaced spots of uniform morphology. Not all deposition or spotting pins designed to the same specifications behave in a similar manner. Each will load an amount characteristic of the pin. Consequently, the size of the first spots produced from a set of pins will be significantly variable. The greatest concern is that

Amendment A
Inventor: Neil A. Winegarden
Attorney Docket No.: 718188.1

deposition of excessive material on the microarrays may yield overlapping spots. The results of which will effect contamination of the material spotted on the arrays as well as the material in the probe plates. As spotting proceeds the excess material is removed and the size of spots become uniform. The purpose of the blot slide or blot pad is to remove the excess material from the pins prior to the spotting on to the microarray slides. This has helped [This has help] ensure the production of well order arrays with uniform spot configuration.

Please replace the paragraph on page 14, lines 25-31 with the following:

The Blot slides are preferably composed of polished glass or similar material. High-quality microscope slides work very well. To maximize the space allocated to the printing of arrays, it is important to determine the minimum size required for the Blot Slide to perform adequately. Sufficient distances are allowed between spotted material to preclude the [preclude and] possibility of overlapping of spots. A centre to centre distance of about 0.5 mm (millimeter) is optimal. Sufficient numbers of spots are printed to ensure uniformity of spots to be subsequently printed on to the arrays.

Please replace the paragraph on page 17, lines 1-4 with the following:

c. The third calibration point is the “down position” (the down position) [(the down position)]. This position is selected to be the point at which the pins are just touching the bottom of the wells (or perhaps a little past the point of touching).

IN THE CLAIMS

Claims 1-17 have been cancelled.

Claims 44-89 have been added as a new claims.